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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/916,780	07/27/2001	Yi Li	883933.0066	9604

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EXAMINER

HELMER, GEORGIA L

ART UNIT PAPER NUMBER

1638

DATE MAILED: 01/02/2003

73

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/916,780

Applicant(s)

LI ET AL.

Examiner

Georgia L. Helmer

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 7-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) ☐ Other: _____

DETAILED ACTION

Restriction election

1. The Office acknowledges the receipt of Applicant's restriction election, Paper No. 11, filed 15 October 2002 Applicant elects Group I claims 1-6, with traverse, stating that Groups II and III are given the same classification, and that therefore, they are the same and do not require separate searches. Applicant's traversal is unpersuasive for the following reasons: Groups II and III have different starting materials and different results and the searches would not be coextensive. The classification data itself is not determining. Therefore, there would be undue burden to search and examine all of the inventions. Claims 1-22 are pending. Claims 7-22 are nonelected. Claims 1-6 are examined in the instant application. Claim 22, which inadvertently was not included in the restriction, is included in the Group III claims. This restriction is made FINAL.

Sequence Listing

2. Applicant's CRF and paper sequence listing have been entered.

Information Disclosure Statement

3. An initialed and dated copy of Applicant's IDS form 1449, Papers No. 6, 7, 8, and 9, dated 15 March 2002, 25 March 2002, 8 April 2002, and 24 June 2002, respectively, are attached to the instant Office action.

Claim Rejections - 35 USC § 112, second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1638

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- In Claim 1, "creation" is not appropriate for a patent claim, as "creation" is usually associated with acts of a deity; "production" is suggested language. "Transiently transgenic plant" is unclear because it describes a plant which is transgenic initially and then become non-transgenic; the instant invention is to a transgenic plant which transiently expresses a trait. Correction is required.
- In 1 (a), "gene" is unclear because a "gene" implies a DNA sequence that exists in nature and includes coding and noncoding regions, as well as all regulatory sequences associated with expression. Since this does not appear to be Applicant's intention, the language "a DNA of interest" is suggested. Or Applicant may recite the various components of the "gene" desired. All recitations of "gene" are also rejected.
- In (iii), "the recombinase-type protein" lacks antecedent basis; also, what is a "recombinase-type protein"? How is it different from a recombinase? "the heterologous DNA" lacks antecedent basis. "DNA excision sequences" is unclear; how do excision sequences differ from non-excision sequences?

- In 1 (c), "the promoter" lacks antecedent basis.

Claim is further unclear because the claim recites a number of DNA sequences which comprise the cassette, but gives no order of the sequences with respect to one another, and with the exception of the promoter of 1 a (iv), does not describe operable relationships of the various DNA sequences.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)):

Nature of the invention. Applicant's claims are drawn to a method of producing a transgenic plant which temporarily convey a phenotypic trait to a plant, comprising constructing a gene cassette comprising a DNA sequence conferring a trait, one or more DNA sequences expressing a recombinase-type protein, at least one pair of DNA excision sequences flanking the heterologous DNA and a transiently active promoter operably linked to the DNA sequence expressing the recombinase –type protein such

Art Unit: 1638

that when the promoter is activated, the recombinase is expressed; introducing the cassette into a plant and expressing the DNA sequences with the cassette to a stimulus that activates the promoter and the recombinase excises the heterologous DNA from the plant genome. Claims are also drawn to gene cassettes comprising a marker gene, transiently active promoters active only in certain organs of the plant, or only at specific stages in the plant's development, or responsive to external stimuli, and to external stimuli comprising chemicals, heat shock, electromagnetic radiation, and exposure to reduced temperatures. The claimed methods use recombinase-type systems to modify gene expression.

State of the prior art. The art is such that the skilled person can introduce genes into plant cells but that generation of a given particular phenotype is unpredictable. Gene expression levels and inheritance are unpredictable (Deroules, SC and Gardner, RC; (1998) Plant Molecular Biology 11: 355-364; Dunwell, JM and Paul, EM (1990) Outlook on Agriculture 19, 103-109; Finnegan J and McElroy D (1994) Bio/Technology 12: 883-888). Organ-specific gene expression in plants is variable (Van-der-Hoeven C et. al. (1994) Transgenic Research 3: 159-166). Recombinase mediated excision of appropriately flanked DNA sequences is variable and yields chimeric phenotypes having both recombined and unrecombined DNA (Gidoni, D. et al, Supplement to Plant Molecular Biology Reporter 18:2, S 03-40; ISPMB abstracts, June 18-24, 2000). Recent studies (Gidoni, D et al (2001) Euphytica 121: 145-156) of embryonal recombination and germline inheritance of recombined tobacco loci show variable recombination efficiencies (Godini 2001, 146 and 152). The claimed methods

require use of recombinase-type systems to delete appropriately flanked DNA sequences.

Breadth of the claims. Claims are broadly drawn to any recombinase, any plant, any trait and any marker gene. Recombinases and recombinase sites are encompassed broadly; Applicant describes site specific recombinases, but claims all recombinases.

Working examples. There are no working examples.

Guidance in the specification. The specification contains three prophetic examples: Prophetic Example 1 describes (p 32) a gene cassette for the reversible introduction of heterologous DNA sequences into a genome of a vegetatively propagated plant. Prophetic Example 2 describes (p 33) a second gene cassette for the reversible introduction of heterologous DNA sequences into a genome of a vegetatively propagated plant. And Prophetic Example 3 (p 35) describes a gene cassette for the reversible introduction of heterologous DNA sequences into a genome of a sexually propagated plant.

Applicant describes a series of steps that one of skill in the art could take to try to produce various desired outcomes. These desired outcomes are all predicated on the ability of a recombinase gene being expressed and successfully excising a DNA specific sequence from a DNA sequence flanked by DNA recombinase excision sequences. If the DNA excision reactions do not function faithfully and at a very high frequency, none of the more complicated steps of the multi-tiered cascade, will function as desired. Applicant gives no specific details of any DNA constructs, nor any results

of use of the various generally described systems to function as desired. Various parameters that need to be defined, such as: what DNA sequence do you put where, in what proximity to other DNA sequences, in what orientation with respect to transcription, in cis or trans configuration to one another, and how large a DNA sequence will function in the various pieces. Applicant offers no information on any of this, other than to list various pieces of DNA which might work in the various desired functions.

Predictability of the art. The physiological art in general is acknowledged to be unpredictable (MPEP 2164.03). Above discussions of the state of the art are repeated below:

The art is such that the skilled person can introduce genes into plant cells but that generation of a given particular phenotype is unpredictable. Gene expression levels and inheritance are unpredictable (Derolles, SC and Gardner, RC; (1998) Plant Molecular Biology 11: 355-364 ; Dunwell, JM and Paul, EM (1990) Outlook on Agriculture 19, 103-109 ; Finnegan J and McElroy D (1994) Bio/Technology 12: 883-888). Organ-specific gene expression in plants is variable (Van-der-Hoeven C et. al. (1994) Transgenic Research 3: 159-166). Recombinase mediated excision of appropriately flanked DNA sequences is variable and yields chimeric phenotypes having both recombined and unrecombined DNA (Gidoni, D. et al, Supplement to Plant Molecular Biology Reporter 18:2, S 03-40; ISPMB abstracts, June 18-24, 2000). Recent studies (Gidoni, D et al (2001) Euphytica 121: 145-156) of embryonal recombination and germline inheritance of recombined tobacco loci show variable recombination efficiencies (Godini 2001, 146 and 152).

Amount of Experimentation necessary. Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden.

Specifically, for any given set of transgenes in a plant, what phenotype is the desired one? For any given set of transgenes, criteria for parameters such as copy number, expression level (RNA or protein) of selectable marker, expression level (or lack of expression) of genes of interest, expression patterns (or lack of expression) of genes of interest, and stability of transgenes through generations, need to be defined. The enablement of creation of a transiently transgenic plant would require an infinite number of variables to be defined and optimized.

In view of the breadth of the claims (to any recombinase, any plant, any trait and any marker gene), the lack of guidance in the specification, and the unpredictability in the recombinase art, undue trial and error experimentations would be required to enable the invention as commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

Art Unit: 1638

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Oliver et al, US 5,723,765, issued March 3, 1998.

Oliver teaches a method comprising constructing a gene cassette comprising a DNA sequence conferring a phenotypic trait, (col 35, lines 33-34), 13-17), a DNA sequence expressing a recombinase-type protein (col 35, lines 22-24), at least one pair of DNA excision sequences cleavable by the recombinase type proteins wherein the excision sequences flank heterologous DNA (col 35, lines 18-20), and a transiently activated promoter operably linked to the DNA sequence expressing the recombinase (col 35, lines 33-34), introducing the cassette into the plant genome (col 35, line 11), and exposing the DNA sequences with the cassette to a stimulus that activates the promoter, expressing the recombinase, and excises the DNA from the genome of the plant (col 42, lines 26-33). Oliver further teaches a marker gene (col 12, line 4), organ specific promoters (col 6, lines 5-16), development stage specific promoters (col 5, lines 65-67), and promoters activated in response to external stimuli, including exposure to a specific chemical species (col 5, lines 38-45).

Accordingly, Oliver anticipates the claimed invention.

Remarks

10. No claim is allowed.

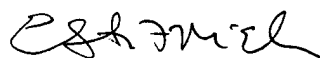
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 703-308-7023. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Georgia Helmer PhD
Patent Examiner
Art Unit 1638, Transgenic Plants
December 26, 2002




ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600